REMARKS

I. Status of Claims

This is in Response to the Final Office Action dated August 11, 2010. A petition for three-month extension of time, a Request for Continued Examination and the corresponding fees accompany this Amendment.

By virtue of the present Amendment, claim 1 has been amended so that the claimed method requires the method to product a composition having a fine particle fraction (MD) of between 40 and 70%. Support for this amendment can be found of page 14, lines 22 to 30 of the international application as filed.

Claims 7 and 13 have been amended to correct the dependencies.

It is submitted that no new matter has been added by virtue of the present amendments.

II. Rejection under § 112, second paragraph

The Examiner rejected claims 7 and 13 as depending from cancelled claims. The dependencies of these claims have been corrected in the present Amendment

III. Rejection under § 102(b) as anticipated by Staniforth (EP 1213012)

In the Office Action, claims 1 and 11-14 were rejected under 35 U.S.C. § 102(b) as anticipated by Staniforth (EP 1213012).

As acknowledged by the Examiner on page 5 of the Office Action, the Staniforth reference fails to teach the velocity of the droplets. For this reason, it cannot anticipate the present claims.

Notwithstanding the above, and solely to expedite prosecution, Applicants have amended claim 1 to additionally recite: "and wherein the composition has a fine particle fraction (metered dose) of between 40 and 70%". The Staniforth patent does not teach the fine particle fraction of

its composition, let alone a fine particle fraction of between 40 and 70%. This is acknowledged by the Examiner on page 9 of the Office Action. For this additional reason, present claim 1 cannot be anticipated by the Staniforth patent. As claims 11-14 depend from claim 1, they also are not rendered anticipated for the same reasons.

Reconsideration of the rejection is respectfully requested.

III. Rejection under § 103

A. Rejection under 35 U.S.C. § 103 over Staniforth in view of Wiedmann

The Examiner rejected claims 1-2, 6 and 11-14 of the present invention under 35 U.S.C. § 103 as being obvious over Staniforth. in view of Wiedmann et al. (Pharm. Dev. & Tech.)

The Examiner states that "the claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the velocity of the droplets at 5 mm from their point of generation is less than 20 m/s." This is inaccurate in that only claim 2 recites this limitation.

The Staniforth patent does not teach or suggest the claimed fine particle fraction of between 40 and 70% found in present claim 1. Further, and as acknowledged by the Examiner, the Staniforth reference teaches that it is preferred that at least 95% by weight of the active particles have a particle size between 0.1 and 5 μm (the size of the particles that constitute the FPF).

The Wiedmann reference cannot cure this deficiency of the Staniforth patent because it also does not teach or suggest the claimed fine particle fraction and, in fact, does not consider or even mention fine particle fraction.

As a result, the combination of the Staniforth reference and the Wiedmann reference cannot render the present claim 1 obvious. As claims 2, 6 and 11-14 depend from claim 1, they also are not rendered obvious for the same reasons.

B. Rejection under 35 U.S.C. § 103 over Staniforth in view of Kodas

The Examiner rejected claims 1, 11-14 and 26 under 35 U.S.C. § 103 as being obvious over Staniforth in view of Kodas (U.S. 6,051,257).

Applicants first point out that the Examiner has incorrectly stated that "the claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the density is greater than 01. g/cc." Applicant does not have this limitation in its currently pending claims.

Notwithstanding the above, Applicants again point out that Staniforth reference does not teach or suggest the claimed fine particle fraction of between 40 and 70% found in present claim 1. The Kodas reference does not mention fine particle fraction, let alone teach or suggest the particular fine particle fraction set forth in the present claims. As such, it cannot cure the deficiency in the Staniforth reference.

Claim 1 therefore is not rendered obvious in view of the combination of the Staniforth reference and the Kodas reference. As claims 11-14 and 26 depend from claim 1, they also are not rendered obvious for the same reasons.

C. Rejection under 35 U.S.C. § 103 over Staniforth in view of Kuo

The Examiner has raised objections to claims 1, 11-14 as being obvious over Staniforth in view of Kuo et al. (U.S. 6518239)

Applicants first point out that the Examiner has incorrectly stated that "the claims are directed to a method of making a dry powder composition for pulmonary inhalation wherein the moisture content of the spray dried particles is adjusted. This is inaccurate in that only claim 15 recites this limitation.

Applicants again point out that Staniforth reference does not teach or suggest the claimed fine particle fraction of between 40 and 70% found in the present claim 1. The Kuo reference does not mention fine particle fraction, let alone teach or suggest the particular fine particle fraction set forth in the present claims. As such, it cannot cure the deficiency in the Staniforth reference.

It is worth pointing out that the the Kuo reference also neither discloses the step of spray drying to produce droplets moving at a controlled velocity nor the use of leucine. Further, the Kuo reference actually teaches away from using leucine by teaching spray-drying of an active with di-leucyl or tri-leucyl-containing peptides to increase the dispersibility of powdered compositions (and without using a means to control the velocity of particles). The Kuo reference indicates that the dispersibility of the di- and tri-leucyl containing powders is better than leucine in improving aerosol performance. The person skilled in the art would therefore have no motivation or reason to use leucine in a dry powder composition and would not consider co-spray drying an active with leucine, as taught in the present invention because the Kuo reference teaches that leucine alone does not provide improved aerosol performance.

The benefit conferred by the claims of the present invention is thought to be a result of the concentration of force control agent on the surface of the spray dried particles obtained by controlled velocity of the spray dried particles, which is reflected in an increase in fine particle fraction compared to the fine particle fraction of particles generated without controlled velocity. The manipulation or adjustment of the spray drying process is thought to result in a co-spray dried force control agent migrating to and concentrating on the surfaces of the particles which are produced. This means that the force control agent will be better able to reduce the tendency of the particles to agglomerate. Such surface concentration also is thought to assist in aerosolisation of the powder particles. The control of the spray drying process takes place

through production of droplets moving at a controlled velocity. In contrast, the method in the Kuo reference purportedly teaches the "uncontrolled" co-spray drying of actives with di- and tri-leucyl peptide to achieve increased dispersibility of the particles. One of skill combining the Kuo reference with the Staniforth reference would have incentive to take the "uncontrolled" co-spray drying and di-leucyl or tri-leucyl-containing peptides of the Kuo reference, which certainly lead away from the presently claimed invention.

In view of the above, Claim 1 is therefore is not rendered obvious by the Staniforth reference in view of the Kuo reference. As claims 11-15 depend from claim 1, they also are not rendered obvious for the same reasons.

D. Rejection under 35 U.S.C. § 103 over Staniforth in view of Tarara

In the Office Action, the Examiner rejected claims 1, 11-14, 25 and 27-29 under 35 U.S.C. § 103 as obvious over Staniforth in view of Tarara et al. (U.S. 6,565,885)

Applicants first point out that the Examiner has incorrectly stated that "the claims are directed to a method of making a dry powder composition for pulmonary inhalation comprising spray-drying heparin and leucine wherein the fine particle fraction is at least 70%. This claim limitation was previously only recited in dependent claim 29, but as now amended, claim 1 recites "wherein the composition has a fine particle fraction (metered dose) of between 40 and 70%".

The Staniforth patent, as explained in its abstract, is directed to:

> A powder for use in a dry powder inhaler comprises active material and additive material. The additive material comprises an anti-adherent material and the powder includes at least 60% by weight of active material. The inclusion of the additive material in the powder has been found to give an increased respirable fraction of the active material.

In contrast, the Tamara reference is purportedly directed to the "delivery of bioactive agents to selected physiological target sites using perforated microstructure powders" and "the formation and use of perforated microstructures and delivery systems comprising such powders, as well as individual components thereof." The Tamara reference further states:

> The disclosed powders may further be dispersed in selected suspension media to provide stabilized dispersions. Unlike prior art powders or dispersions for drug delivery, the present invention preferably employs novel techniques to reduce attractive forces between the particles.

The background of the Tamara reference discusses the prior art technology employing fine particles combined with larger carrier particles used to overcome agglomeration and argues that its use of perforated microstructures overcomes the problems of the prior art, e.g. when fine particles attach to the larger carrier particles and deposit in the throat, because its perforated microstructures purportedly have significantly reduced attractive forces between them, and therefore better dispersibility. The Tarara reference therefore teaches an alternative solution to the problem of providing particles with improved dispersibility than that of either Staniforth or the presently claimed invention.

Further, the Staniforth reference teaches that a high FPF is preferable (e.g. where at least 95% of the particles having a particle size between 0.1 and 5μm. In contrast, the Tamara reference suggests that a lower FPF can be used. Further, the Tamara reference does not disclose or suggest the step of spray drying which includes producing droplets moving at a controlled velocity, does not disclose heparin as an active agent or leucine as a force control agent.

The Tamara also teaches that, although spray drying is preferable, other techniques can be used to create its perforated microstructures such as vacuum drying, solvent extraction, emulsification or lyophilization, and combinations thereof, which is again, contradictory to the teachings of the Staniforth patent. When spray drying is used in the Tamara reference, it is

preferably used in conjunction with a blowing agent, yet again, a teaching contradictory to that of Staniforth.

It would be readily apparent to one of skill in the art that the Tamara reference teaches away from formulations like the Staniforth reference. One of skill would have no incentive to combine references having such disparate teachings and the combination would not likely result in the specific method of claim 1, having e.g. the claimed controlled velocity of the droplets, the use of heparin as an active agent, leucine as a force control agent or the claimed fine particle fraction of 40-70% of the present invention. Only though the use of improper hindsight can the fine particle fraction of the Tamara reference be cherry picked out and deposited into the Staniforth reference, as one of skill in the art has been provided no reason to do so by the teachings of either reference.

Claim 1 therefore is not rendered obvious by the combination of the Staniforth reference in view of the Tarara reference. As claims 11-14, 25 and 27-29 depend from claim 1, they also are not rendered obvious for the same reasons.

In view of the foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

Conclusion

This Response is being submitted in response to the Office Action dated August 11, 2010 in the above-identified application. Concurrently with this Response, Applicants submit a petition for three-month extension of time for filing a response, a Request for Continued Examination and the corresponding fees. If it is determined that any additional fee is due in connection with this filing, the Commissioner is authorized to charge said fees to Deposit Account No. 50-0552.

An early and favorable action on the merits is earnestly requested.

Respectfully submitted,
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